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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO..
10/664,422	09/17/2003	Guy A. Rouleau	GOUD:023USD3	3964

7590 10/09/2007

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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
10/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,422	ROULEAU ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,17,20 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,17,20 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/27/07, 5/2/07, 5/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 27 July 2007 have been entered. Claims 1 – 13, 15 – 16, 18 – 19, 21 – 22, and 26 – 28 are canceled. Claims 14, 17, 20, and 23 – 25 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 July 2007 has been entered.

Withdrawn Rejections and Objections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. Any rejection of, or objection to, a canceled claim is now moot.

B. The rejections of record under 35 USC 112, second paragraph are withdrawn in light of the amendments. However, note the new rejection of claim 25 under 35 USC 112, second paragraph below necessitated by the amendments to the claims.

C. The rejection under 35 USC 102(b) over Lu is withdrawn in light of the amendments. The claims now require at least 95% identity to either SEQ ID NO:65 or the full-length complement thereof; previously the claims included fragments as well. The prior art reference by Lu is outside the scope of the instant claims.

Maintained Rejections and Objections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 17, 20, and 24 – 25 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids at least 95% identical to SEQ

ID NO:65 which encode sodium channels, does not reasonably provide enablement for nucleic acids at least 95% identical to SEQ ID NO:65 as broadly claimed, and does not reasonably provide enablement for the full scope of nucleic acids "wherein the presence of said nucleic acid in a sample of a subject indicated that the subject has an increased risk of idiopathic generalized epilepsy" as recited in claim 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection stands for the reasons previously made of record. SEQ ID NO:65 encodes a human sodium channel. Parts (a) and (b) of claim 14 are enabled over their entire scope. However, part (c) of claim 14 is not enabled over its full scope. The prior art of record recognized that sodium channels are useful proteins, and that they are crucial in propagation of action potentials. The specification discloses many possible uses of sodium channels, and notes that there are several activities that are common to sodium channels (see for example paragraph spanning pp. 19 – 20). It is within the skill of the artisan to determine how to make and how to use variants of SEQ ID NO:65 which both retain 95% sequence identity and which encode sodium channels. However, claim 14 encompasses variants of SEQ ID NO:65 with any function at all or with no function whatsoever. There is no requirement that any particular structural elements be retained, there is no requirement that the nucleic acid variants have any particular function on their own, and there is no requirement that the nucleic acid variants encode functional sodium channels. Claim 14 encompasses nucleic acids that encode the N-terminal methionine of the encoded protein, followed by a stop codon, and the remainder of SEQ ID NO:65. Clearly such a nucleic acid could not be used as disclosed, as it would encode a totally nonfunctional protein.

The prior art of record (Rudinger, cited in office action mailed 21 August 2006) indicates that it is very difficult to assign function to specific amino acids within protein sequences (see also Honig, cited in office action mailed 27 April 2007). Applicant is directed to the previously-mailed office actions for a more thorough discussion of this matter. Changing the nucleic acid sequence would be expected to lead to mutated non-functional proteins. The specification does not disclose to the skilled artisan how to use those nucleic acids which do not encode sodium channels. Claim 14, part (c) encompasses nucleic acids 95% identical to the complement of SEQ ID NO:65, but the specification does not disclose how to use the full scope of such nucleic acids. As the claim reads on a very large number of possible nucleic acid sequences for which

enablement has not been demonstrated, and because the specification fails to provide guidance in determining how to use those nucleic acids which do not encode functional sodium channels, claim 14 clearly reads on an unreasonably large number of possible sequences that could not be used in the absence of a great deal of experimentation. The skilled artisan would essentially have to determine, on his or her own, how to use those nucleic acids which do not encode functional proteins. Given the paucity of guidance and the lack of working examples on point to nucleic acids which do not encode sodium channels, the large degree of experimentation required to make and use the full scope of claim 14 would clearly be undue. In order to expedite prosecution, it is recommended that applicant amend claim 14 part(c) to read "...95% identity to SEQ ID NO:65, wherein the nucleic acid encodes a sodium channel".

Claims 17 and 20 are rejected as they depend from claim 14 but are not limited to enabled embodiments. Claim 24 also is drawn to a large number of possible sequences for which enablement has not been demonstrated and which the skilled artisan could not make in the absence of undue experimentation. The specification fails to disclose to the skilled artisan the full scope of the nucleic acids which are indicative of an increased risk of epilepsy. While a few mutations in SCN3A-encoding nucleic acid are reported at pp. 53 – 54 of the specification, such disclosure is not commensurate in scope the breadth of claim 24. Claim 24 only requires 95% sequence identity to SEQ ID NO:65, as it depends from base claim 14. There is no requirement that any particular region of the nucleic acid be conserved or present. There is no requirement for mutation at any particular nucleotide. Thus the skilled artisan would have to determine which nucleotide positions within SEQ ID NO:65 are indicative of the subject having an increased risk of epilepsy. Given that SEQ ID NO:65 is over 9000 nucleotides long, a great deal of experimentation would certainly be necessary in order to determine which positions are indicative of increased risk. Wallace (US 7,078,515) teaches that single base pair changes within sodium channel sequences do not result in an increased risk of epilepsy, as some of these polymorphisms are found equally often in control patients and those with epilepsy (Wallace, column 17 lines 52 – 58). While Wallace is on point to sodium channel 1a rather than 3A sequences as instantly-claimed, in both cases the inventions are drawn to changes in nucleic acid sequences which encode sodium channels and resultant changes in likelihood of having epilepsy. Thus the effects of changing nucleic acid sequences in sodium channel genes on risk for epilepsy is unpredictable. Coupled with the relatively small disclosure of positions

which in fact confer increased risk of epilepsy to subjects, the large amount of experimentation required to make the full scope of nucleic acids of claim 24 would clearly be undue.

Claim 25 depends from rejected claims and is therefore rejected as well. While certain specific nucleotide positions are recited, claim 25 ultimately depends from claim 14, which is not enabled over its full scope as set forth above. Thus claim 25 encompasses nucleic acids which do not encode proteins and for the reasons set forth above the skilled artisan could not make and use the full scope of the invention of claim 25 in the absence of undue experimentation.

5. Claims 14, 17, 20, and 24 – 25 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification fails to describe to the public the full genus of nucleic acid sequences encompassed by claim 14. Claim 14, part (c), encompasses nucleic acids at least 95% identical to SEQ ID NO:65 or to the full-length complement thereof. Claim 14 part(c) does not require that any particular structural element be present in the nucleic acid sequence. The skilled artisan cannot immediately visualize those structures which are common to all members of this genus. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

In the instant case, the specification discloses SEQ ID NO:65 and a few mutants. However the specification fails to describe all nucleic acid sequences at least 95% identical to SEQ ID NO:65. Applicant is directed the Revised Written Description Interim Guidelines Training Materials, available on the internet at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>, which is analogous to the instant situation. See particularly Example 14, which indicates that claims to biological sequences which also recite relevant function can be considered to be adequately described. Amendment of claim 14 part(c) to read "..."...95% identity to SEQ ID NO:65, wherein the nucleic acid encodes a sodium channel" may help advance prosecution.

Claims 17 and 20 are rejected as they depend from rejected claim 14 but are not limited to those members of the genus which could reasonably be considered to be fully described. Claim 24 is also not fully described. The specification fails to disclose to the public those structures which are required for the claimed nucleic acids, and fails to set forth the positions within SEQ ID NO:65 which, when altered, lead to "an increased risk of idiopathic generalized epilepsy" as claimed. While certain examples falling within the scope of this genus are described, the full genus has not been described. SEQ ID NO:65 is over 9000 nucleotides long; disclosure of a handful of single nucleotide polymorphisms cannot reasonably be considered to indicate that applicant was in possession of the full genus of nucleic acids which, when present in a sample of a subject, indicate increased risk of this form of epilepsy.

Claim 25 depends from rejected claims and is therefore rejected as well. While certain specific nucleotide positions are recited, claim 25 ultimately depends from claim 14, which is not fully described as set forth above. Thus claim 25 encompasses nucleic acids which do not meet the written description requirement for the reasons set forth above the skilled artisan could not immediately envision the genus of products encompassed claim 25.

6. Claim 25 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

This rejection stands for the reasons previously made of record and reiterated below. Claim 25 refers to mutations at specific nucleotide positions within SEQ ID NO:65 that the specification as originally filed does not disclose. See office action mailed 27 April 2007, pp. 11 – 12. Applicant argues, on pp. 4 and 6 – 7 of the remarks filed 27 July 2007 that the specification provides evidence of possession of the specific mutations recited in claim 25. Applicant points to pages 53 – 54 and Figure 7 of the disclosure as originally filed as providing the relevant support.

Applicant's arguments have been fully considered but they are not persuasive. The cited pages of the specification disclose the result of PCR experiments which indicate applicant had found two DNA mutations which lead to two specific protein changes. The first is a DNA mutation whereby the nucleotides AAT are skipped, resulting in deletion of amino acid residue 43. The second is a single nucleotide polymorphism which changes amino acid residue 1035 from valine to isoluceine (specification, pp. 53 – 54). No corresponding nucleic acid numbers are provided in the specification. Neither mutation is disclosed as being at residue 759 – 761 or 3735 of SEQ ID NO:65, as recited in claim 25.

The skilled artisan would have a sound scientific basis for concluding that the mutations which lead to the deletion or change in amino acid, described on pp. 53 – 54 of the specification, are in fact not encoded by changes at the cited nucleotide numbers. The genetic code results in three nucleotides encoding a single amino acid. The specification fails to identify where the start of the protein-coding region of SEQ ID NO:65 is. If it were at the beginning of the sequence, amino acid residue 43 would be 129 nucleotides in to the sequence and would not be encoded by residues 759-761 as recited in claim 25. Amino acid 1035 would be encoded by a codon starting at nucleotide 3105, not 3735 as recited in claim 25.

The art recognizes at least two other human SCN3A-encoding sequences. These are available as NCBI accession numbers NM_001081676 and NM_001081677, respectively (see enclosed printouts). Each is of approximately the same length as applicant's SEQ ID NO:65, and encodes a 1951 amino acid protein, exactly the same length as applicant's SEQ ID NO:67.

In each of these publicly available sequences, the coding sequence begins at nucleotide 493. In those sequences, residue 43 is encoded by a codon starting at nucleotide 622, residue 1035 is encoded by the nucleotides starting at residue 3598. Thus the skilled artisan would most likely conclude that the mutations are at nucleic acids 622 and 3598, not 759 and 3735 as recited in claim 25.

While it is without question that applicant was in possession of the small fragments of nucleic acid surrounding mutated bases as identified in the PCR and SSCP analyses described on p.. 53 – 54, the examiner is unable to find disclosure of nucleic acids at least 95% identical to SEQ ID NO:65 wherein there is either a deletion mutation at positions 759 – 761 or a G to A mutation at position 3735, as recited in claim 25.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 17, 20, and 23 – 24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Clare et al. (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York NY May 14 – 17, 1998, published as Annals of the New York Academy of Sciences 1999. 868:80-83, of record).

This rejection stands for the reasons of record. Briefly, Clare teaches an isolated nucleic acid encoding human SCN3A protein, which is approximately 9.5 kb in size (note the ~ character on the figure indicates the size is approximate), as well as vectors and host cells comprising same. Applicant is claiming three types of nucleic acid in claim 14: molecules comprising SEQ ID NO:65, molecules comprising the full-length complement thereto, and molecules comprising sequences at least 95% identical to either of those. As set forth previously, the office does not have the resources or facilities to determine the sequences of the nucleic acids isolated by Clare. Applicant states, on p. 9 of the remarks filed 27 July 2007, that he is unable to obtain the nucleic acid and sequence it. While the burden to distinguish the claimed invention from the prior art product which appears to be identical is on applicant (MPEP

§ 2112(V)), applicant has chosen not to provide evidence that there is a patentably distinct difference between the two.

The prior art product is an isolated nucleic acid encoding human type III sodium channel. The claimed invention is an isolated nucleic acid encoding human type III sodium channel. The prior art is silent as to the sequence of the isolated nucleic acid, but the sequence is an inherent property. Discovering a new property, such as a sequence, of an old product does not render the product patentable (see MPEP § 2112(I)). As the claims encompass a prior art product that is identical except for a feature which appears to be an inherent property, and there is no evidence of record indicating a novel and non-obvious difference between the prior art and the claimed invention, the rejection of record stands.

Applicant makes the following arguments as to how the claimed invention might be different from the prior art:

1) the prior art product is listed as being ~9.5 kb in size, whereas applicant's SEQ ID NO:65 is 9.1kb.

2) Clare is an unenabling disclosure because the reference does not disclose the sequences.

Applicant's arguments have been fully considered but they are not persuasive. With respect to 1) above, it is important to note that the size reported in Clare is clearly approximate (note use of "~" symbol). The size was deduced from the position on the Northern blot, which does not have single-base-pair resolution. The size may well be slightly different from 9.5kb. Additionally, applicant is specifically claiming nucleic acids which comprise SEQ ID NO:65, or those 95% identical thereto. The use of open ("comprising") claim language in the preamble of claim 14 clearly indicates applicant is claiming those molecules which have additional nucleic acid sequences added on either end. Thus even if the prior art sequence is slightly longer than 9.1kb, it is still within the scope of these claims, which use open claim language.

With respect to 2), applicant argues that Clare is not enabling because the reference does not disclose the sequence. However, knowing the nucleic acid sequence is not required to make the invention. Clare clearly shows how to isolate the claimed invention, for example on a Northern blot. The instant claims are not drawn to methods of making nucleic acid molecules by assembling single nucleotides in a particular order, for which knowledge of the sequence would clearly be necessary. The claims are directed to the isolated nucleic acid product, which can be made either by such synthetic techniques or by isolating the product from nature. Thus the fact

that Clare fails to disclose the sequence does not indicate the reference is non-enabling. Rather it indicates that the claimed products can be made by more than one process.

For the reasons above and those previously made of record in earlier office actions, the rejection over Clare stands.

New Rejections

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites the limitation "said alpha subunit of a sodium channel" in lines 1 – 2. There is insufficient antecedent basis for this limitation in the claim. Additionally, the claim is confusing because it appeats that a nucleic acid sequence also is a protein.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Patent Examiner
Daniel E. Kolker, Ph.D.
October 1, 2007